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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,397	01/14/2004	Sharon Cohen-Vered	2609/68811-A/JPW/GJG/JBC	6066

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EXAMINER	
AUDET, MAURY A	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,397	COHEN-VERED ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16,24,25,27,31,36,37,47 and 52* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1-13,16,24,25,27,31,36,37,47 and 52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response of 4/10/07 is acknowledged. It was noted by the Examiner that claim 36 was not addressed by the Examiner on the previous Form 326 (cover sheet), as being rejoined or not, or within substantive rejections (other than the 35 USC 112 2nd) – and it was not indicated as allowable. Additionally, Applicant did not substantively address claim 36 (except as to the 35 USC 112 2nd rejection). Thus, the previous action is being resent in it's entirety and as to the previously amended claims (other than the considered IDS's) to address claim 36 – underlined below where previously omitted - in the event Applicant felt it was necessary to address the limitations of this claim under the other statutory grounds of rejection (if not necessary, all Applicant need do it input claim 36 in the response where needed and refile the previous response – Applicant may also file anything further deemed relevant (amendment/ arguments)). The action is being sent NON-FINAL, in order to clarify the record. The substance of Applicant's 4/10/07 response will be fully addressed at the next response date.

Election/Restrictions

Applicant's election with traverse of Group I, current claims 1-13, 24-25 and 52, as drawn to the elected invention peptide SEQ ID NO: 6, in the reply filed on 07/31/2006 is acknowledged. The Examiner has rejoined claims 16, 27, 31, 36-37, and 47. The only currently non-rejoined Group, is Group II (claim 14 (method of use)). As to the traversal of the Groups, the traversal is deemed moot, as there was no traversal for the restriction between Group II and the other Groups (e.g. elected Group I). Applicant's remaining traversal is of the peptide election as the invention, namely, that all the distinct sequences corresponding to SEQ ID NO:

16 should be searched, and can be without an undue burden. This is not found persuasive for the reasons of record, and would pose a substantial undue burden, as described in the Restriction Requirement. Claim 14 is withdrawn as being drawn to a non-elected invention. Claims 1-13, 16, 24-25, 27, 31, 36-37, 47, and 52 are examined on the merits, as drawn to the elected peptide, comprising SEQ ID NO: 6.

*It is noted at the outset (as discussed in the Provisional Obvious Double Patenting Rejection below), that the claims of this application and co-pending US 10/758,572, and the elected inventions thereto, are virtually identical. The rejections made and maintained in the '572 are very similar, though the claim numbers may differ.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claims 1-13, 16, 24-25, 27, 31, 36-37, 47, and 52 are objected to because of the following informalities: the claims have not been amended to be commensurate in scope with the elected invention (namely elected peptide of the invention, comprising SEQ ID NO: 6). Appropriate correction is required.

Claims 1 and 11 are objected to because of the following informalities: In claims 1, and 12, the last phrase describes a "composition", suggest the claim state, "... the pharmaceutical composition has a pH..." as recited in the preamble of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 8-9, 13, 16, 24-25, 27, 31, 36-37, 47, and 52 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Mozes (U.S. 2004/0127408 A1 (Priority date = February 26, 2001)) in view of Hora et al. (U.S. Patent 5,997,856).

Mozes discloses peptides and pharmaceutical compositions (for the treatment of systemic lupus erythematosus). Mozes discloses a 19-mer peptide sequence identified as SEQ ID NO: 6, which has 100% identity with current application SEQ ID NO: 1 (see U.S. Publication '408, paragraphs 21, 67, and claims 2, and 9). Mozes does disclose the salt of the peptide, including an acetate salt (see U.S. Publication '408, paragraphs 15, 88, and claim 1). Mozes discloses a pharmaceutical composition comprising the peptide and a pharmaceutically acceptable carrier (see U.S. Publication, '408, claims 24, and 25). Mozes does not explicitly disclose a pharmaceutical composition comprising a pharmaceutically acceptable salt of a peptide and a substituted beta-cyclodextrin.

Hora et al. disclose the solubilization and/or stabilization of polypeptides, especially proteins, using cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl, and maltotriosyl derivatives of beta-cyclodextrin (see entire document, particularly col. 11, line 59 through col. 12, line 17). Hora et al. disclose protein, hydroxypropyl beta-cyclodextrin compositions that have proteins at concentrations ranging from 0.25 mg/ml to

1 mg/ml (see U.S. Patent '856, col. 22, Table 2). Hora et al. also describes a lyophilized composition comprising a polypeptide and a stabilizing/solubilizing amount of cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of beta-cyclodextrin (see U.S. Patent '856, col. 12, lines 10-15, and col. 2, Table 2, column describing type).

One would have been motivated to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide disclosed by Mozes with the beta-cyclodextrin derivatives disclosed by Hora et al., because of the enhanced solubilization and stabilization of the peptide in the beta-cyclodextrin derivative solution. Therefore, it would have been obvious to the person having ordinary skill in the art to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide identified as SEQ ID NO: 1 that is disclosed by Mozes, along with the beta-cyclodextrin derivatives disclosed by Hora et al. (to treat systemic lupus erythematosus). Furthermore, it would have been obvious to the person having ordinary skill in the art lyophilize the composition comprising the peptide disclosed by Mozes, and the beta-cyclodextrin derivatives disclosed by Hora et al., because Hora et al. disclose a lyophilized polypeptide/beta-cyclodextrin composition.

Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes (U.S. 2004/0127408 A1 (Priority date = February 26, 2001)) in view of Hora et al. U.S. Patent 5,997,856 as applied to claim 1-4, 7, 8, 11, 31, 42, 53, 57, and 59-61 above, and further in view

of Anderson and Flora (Chapter 34, pages 739-754, The Practice of Medicinal Chemistry, edited by Camille Georges Wermuth, Academic Press 1996).

Mozes and Hora et al. do not explicitly disclose a pharmaceutical composition having a pH between 6.5 and 8.5. Anderson et al. disclose the ideal pH for injectable formulations to be the pH of blood, 7.4, while pH above 9 causes tissue necrosis, and pH below 3 causes extreme pain and phlebitis (see page 747, 3rd paragraph).

One would have been motivated to manufacture a pharmaceutical composition within the range of pH being between 6.5 and 8.5 to be able to administer an injectable pharmaceutical composition. Therefore, it would have been obvious to the person having ordinary skill in the art to manufacture a pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide identified as SEQ ID NO: 1 that is disclosed by Mozes, along with the 13-cyclodextrin derivatives disclosed by Hora et al. with a pH between 6.5 to 8.5 (to treat systemic lupus erythematosus).

Claims 6-7 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. (2004/0127408 A1 (Priority date = February 26, 2001)) in view of Hora et al. (U.S. Patent 5,997,856), and further in view of Stella et al. (U.S. Patent 5,134,127).

Mozes and Hora et al. do not disclose a pharmaceutical composition comprising a sulfobutyl ether substituted beta-cyclodextrin. Stella et al. disclose the use of sulfoalkyl ether cyclodextrin derivatives as solubilizing agents for water insoluble drugs for oral, intranasal, or parenteral administration (see U.S. Patent '127, Abstract). Stella et al. disclose the use of sulfobutyl ether substituted beta-cyclodextrin complexed to digoxin, progesterone, testosterone,

and phenytoin (see U.S. Patent '127, Figure 4, 5, 7, 9, Tables 2-5, col. 14, line 35 - col. 15, line 17, and claim 8).

Applicant is also referred to MPEP 2144.05 Obviousness of Ranges. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.");< ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocrafl Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

One would have been motivated to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide disclosed by Mozes with the sulfobutyl ether substituted beta-cyclodextrin derivatives disclosed by Stella et al., because of the enhanced aqueous solubilization, reduced toxicity, and reduced membrane disruption of the sulfobutyl ether substituted beta-cyclodextrin derivative solution (see U.S. Patent '127, col. 3, line 9-16). Therefore, it would have been obvious to the person having ordinary skill in the art to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide identified as SEQ ID NO: 1 that is disclosed by Mozes, along with the beta-cyclodextrin derivatives disclosed by Stella et al. (to treat systemic lupus erythematosus).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-13, 16, 24-25, 27, 31, 36-37, 47, and 52 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18, 21, 31-32, 41, 52-53, and 57-61 of copending Application No. 10/758,572. Although the conflicting claims are not identical, they are not patentably distinct from each other because virtually the identical claims and products, comprising SEQ ID NO: 2 are claimed. (However, the '572 is much further along in examination/prosecution and has been through two Non-Final Actions, a Final Action, and numerous amendments which have slightly varied the two claim sets).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 27, ***36,*** 37, 47, and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In e.g. claims 16 and 27, in step a), what is the "predetermined concentration"?

In e.g. claims 16 and 27, in step a), how long is the temperature maintained at -40°C, and -45°C, respectively? In steps b), d), and e), what is the "predetermined time"? In step e), what is the reduced pressure that lyophilizes the pharmaceutical composition?

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 07/07/2007

MAURY AUDET
PATENT EXAMINER